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08/619,649	03/27/1996	RADOJE DRMANAC	ARCD:146/BOW	7575

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^{12/15/2009}
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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

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12/15/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

08/619,649

Applicant(s)

DRMANAC, RADOJE

Examiner

BJ Forman

Art Unit

1634

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 97 and 157-176 is/are pending in the application.
- 4a) Of the above claim(s) 176 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 97 and 157-175 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/02)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 20 October 2009 in which the previous rejections were traversed. The arguments have been thoroughly reviewed and are discussed below.

The previous objection to the claims in the Office Action dated 20 April 2009 is withdrawn in view of Applicant's comments on pages 7-8 of the response. The previous rejections under 35 U.S.C. § 103 are maintained.

Claims 97 and 157-175 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 97, 157-175 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (Genomics, 1992, 13: 1008-1017) in view of Brigati (U.S. Patent No. 4,777,020, issued 11 October 1988) or Augenlicht (U.S. Patent No. 4,981,783, issued 1 January 1991).

Regarding Claims 97, 157-158 and 166-168, Southern discloses a support comprising an array of four microchips, each having an array of oligonucleotide probes immobilized thereon (Fig. 3, figure legend, line 1).

Southern teaches each array is in one of four quadrants on the surface (Fig. 3). The four-quadrant arrangement is encompassed by the physical separation because a quadrant defines a physical location of the surface. Assignment of an array to a quadrant defines a boundary between quadrants, the boundary being the point of physical separation. While the reference specifically teaches that the arrays are physically separated, Southern does not specifically teach a physical barrier. However, physical and hydrophobic barriers separating hybridization regions were well known and routinely practiced in the art at the time the instant invention was made as taught by Brigati who teaches that the groove and hydrophobic barriers provide for comparative analysis of hybridization to the same probes to different samples and/or hybridization of different probes to the same sample (Column 9, line 63-Column 10, line 15).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Brigati to the multiple arrays of Southern. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the benefit of comparative analysis of the multiple arrays to different samples as desired in the art (Brigati, Column 9, line 63-Column 10, line 15).

Furthermore, Augenlicht teaches multiple arrays on a support separated by a physical barrier i.e. spacing between membranes (Fig. 1) whereby side-by-side analysis

and comparison of separately prepared arrays is provided (Column 7, lines 18-47). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrays of Southern by spatially separating the arrays as taught by Augenlicht. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the benefit of providing side-by-side analysis and comparison of separately prepared arrays as desired in the art (Augenlicht, Column 7, lines 18-47).

Regarding Claims 159 and 169, Southern discloses the support wherein the microchips are arranged in multiple rows and columns (i.e. two rows and two columns, Fig. 3). And Brigati discloses the support comprising multiple rows and columns (e.g. 30 slide pairs providing 2 rows of 30 columns, Column 7, lines 44-45).

Regarding Claims 160 and 170, Southern discloses the support wherein the microchips are positioned for use with a multichannel pipette (Fig. 3). The arrays of Southern are arranged in two rows of two columns. While Southern does not teach use of a multichannel pipette, the courts have stated that a claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. *Ex parte Masham*, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987). Southern teaches the structural elements of the claim and therefore, teaches the support of Claims 160 and 170.

Regarding Claim 161 and 171, Brigati discloses the device wherein the device comprising assay ingredients e.g. labeled sample (Column 10, lines 8-15).

Regarding Claims 162 and 172, Southern teaches a 4 by 4 array but does not teach an 8 by 12 array. Brigati teaches the microchips wherein the nucleic acids are spotted in defined positions on the slides (Column 10, lines 8-15) but is silent regarding the an 8 x 12 format of spotted probes.

Furthermore, spotting probes in an 8 x 12 format was well known and routinely practiced in the art at the time the invention was made as taught by Augenlicht. Augenlicht further teach the format utilizes commercially available spotting pins that are useful for making replica arrays from multiwell cultures and produce precisely defined positions. (Column 6, lines 17-28 and Column 13, lines 55-60). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 8 by 12 format of Augenlicht to the arrays of Southern and/or Brigati for the expected benefit of providing precisely defined and replicated regions as desired in the art (Augenlicht, Column 13, lines 55-60).

Regarding Claims 163 and 173, Southern discloses the support wherein the array of microchips comprises more than 256 probes i.e. each of the four microchips has 256 probes. Hence, the support of Claim 97 has more than 256 probes per array as claimed.

Regarding Claims 164 and 174, Southern discloses the support wherein the probes are between 4 and 9 bases (Fig. 3).

Regarding Claims 165 and 175, Southern discloses the support wherein the probes are synthesized on the support (page 1009, left column). Southern does not teach light-directed synthesis. However, the courts have stated that "even though

product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because Southern teaches the product, the process of making the product as recited in the claim does not define the product over that of Southern.

4. Claims 97, 157-175 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac et al (Electrophoresis, 1992, 13:566-573) and Hardy et al (U.S. Patent No. 4,681,853, issued 21 July 1987).

Regarding Claims 97, 157-158 and 166-168, Drmanac discloses a support comprising multiple microarrays (Fig. 4), each comprising an array of differing oligonucleotides immobilized thereon wherein the microarrays are separated from each other. The arrays illustrated in Fig. 4 clearly appear to be separated by a barrier, and the reference teaches that hybridization with different samples requires separation (page 571, last paragraph). The reference does not specifically teach physical barriers. However, physical barriers grooved and/or hydrophobic were well known in the hybridization art at the time the invention was made as taught by Hardy (Fig.1).

Hardy teaches a similar support comprising a plurality of arrays, each comprising differing oligonucleotides (Column 4, lines 17-56) wherein the arrays are separated by a physical groove and/or hydrophobic strip (Column 4, lines 39-56) whereby hazardous and/or costly materials are handled safely and efficiently (Column 4, lines 10-16).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Hardy to the multiple arrays of Drmanac. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the expected benefit of providing for safe and efficient handling of hazardous and costly materials as desired in the art (Hardy, Column 4, lines 10-16).

Regarding Claims 159 and 169, Drmanac teaches the support wherein the microchips are arranged in multiple rows and columns (Fig. 4). And Hardy teaches the similar support comprising multiple rows and columns (Fig. 1).

Regarding Claims 160 and 170, Drmanac teaches the support wherein the microchips are "positioned" for use with a multichannel pipette (i.e. arrayed, Fig. 4). Hardy teaches the similar support wherein the microchips are "positioned" for use with a multichannel pipette (i.e. arrayed, Fig. 1).

Regarding Claim 161 and 171, Drmanac teaches hybridization reagents (page 571). Hardy teaches the similar support and hybridization reagents (Column 11).

Regarding Claims 162 and 172, Drmanac teaches the arrays are arrayed in 8 by 12 format (paragraph spanning pages 569-570).

Regarding Claims 163 and 173, Drmanac teaches the support wherein the array of microchips comprises more than 256 probes (page 569-570).

Regarding Claims 164 and 174, Drmanac teaches the support wherein the probes of between 4 and 9 bases are spotted onto the arrays for hybridization (page 571).

Regarding Claims 165 and 175, Drmanac teaches the support of Claims 97 and 166 as discussed above. While the reference does not teach light-directed synthesis. However, the courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because the combination of Drmanac and Hardy teach the product, the process of making the product as recited in the claim does not define the product over the prior art.

Response to Arguments

5. Applicant acknowledges that Southern teaches 4 arrays on the support, but asserts that the arrays of Southern are not microchips as claimed. Applicant further acknowledges that Southern teaches physical separation but argues that the separation

is not a physical barrier or hydrophobic surface as claimed. Applicant argues that Southern does not teach or suggest that separate hybridization reactions can be carried out with the four separated arrays. Applicant further asserts that Brigati fails to cure this deficiency because the reference fails to suggest that antigens on different slide can be tested simultaneously against different samples. Applicant argues that Augenlicht also fails to suggest that separated filters can be tested simultaneously against different samples. Applicant asserts that the instantly claimed invention provides an advantage over the art i.e. "the ability to carry out a large number of assays at the same time in individual arrays separated by physical barriers or hydrophobic surfaces". Applicant further asserts that the specification teaches this significant advancement.

The arguments have been considered but are not found persuasive. Applicant has not identified any structural element that is missing from the combined teachings of Southern, Brigati and/or Augenlicht. It is maintained that all the elements were known as cited above. Applicant's arguments appear to focus on the advantages provided by the instant invention i.e. "the ability to carry out a large number of assays at the same time in individual arrays separated by physical barriers or hydrophobic surfaces"... allowing for a heretofore unattainable amount of data accumulation". Applicant asserts that the specification teaches these significant advancements. On pages 5-6 of the response, Applicant points to pages 16 and 40-42 of the specification for teaching the advantages of the claimed invention. The cited passage of page 16 describes separated arrays but describes no unexpected advantages and is silent regarding a "large number of assays" or "amount of data accumulation".

...multiple arrays of immobilized oligonucleotides arranged to form a so-called "sequencing chip" One example of a chip is that where hydrophobic segments are used to create distinct spatial areas.

The cited passage of pages 40-42 describes the well known grid filter assays and problems solved by the instant invention.

Two basic problems have to be solved. Manipulation with small (2-3 mm) chips, and parallel execution of thousands of the reactions. The solution of the invention is to keep the chips and the probes in the corresponding arrays. In one example, chips containing 250,000 9-mers are synthesized on a silicon wafer in the form of 8x8 mM plates (15 uM/oligonucleotide, Pease *et al.*, 1994) arrayed in 8x12 format (96 chips) with a 1 mM groove in between. Probes are added either by multichannel pipet or pin array, one probe on one chip. To score all 4000 6-mers, 42 chip arrays have to be used, either using different ones, or by reusing one set of chip arrays several times. (emphasis added).

Based on the cited passage, the advantages provided by the invention are 1) manipulation with 2-3mm chips and 2) parallel execution of thousands of reactions. To obtain these advantages, probes are arrayed "one probe on one chip". Hence, three structural elements are required to obtain the asserted advantages: 2-3mm chips, thousands (arrays or probes or chips), and one probe on one chip. None of these three elements are limitations of the claims. Furthermore, neither Applicant's response nor the specification provides evidence of the asserted advantages obtained using the instantly claimed invention.

Furthermore, it is maintained that Brigati teaches the advantages of multiple assay performance using the separated regions of different immobilized targets. Applicant's assertion that the reference does not teach a combination of different targets tested against different samples is not relevant to the instantly claimed invention because the tested samples are not defined, described or required in the instantly

claimed invention. The claims merely require different oligonucleotides attached to different locations, which is taught by Southern, Brigati and Augenlicht. Therefore, arguments regarding samples applied are not commensurate in scope with the claims. It is maintained that all of the structural elements required by the claims are taught and described by the prior art as cited above.

Regarding the combination of Drmanac and Hardy, Applicant the references suffer the same deficiencies as Southern, Brigati and Augenlicht and states that the disclosures of Drmanac is similar to that of Southern in that the multiple arrays are hybridized to the same sample. Applicant argues that even if the arrays of Drmanac are separated, the separation is not sufficient for parallel assays against different samples.

The arguments have been considered but are not persuasive for reasons similar to those above. The claims do not define a support for multiple parallel analysis of different samples and do not define any structural elements over the prior art. Furthermore, no evidence has been provided to support assertion of "unrealized advantages". Therefore, the argument is deemed unsupported arguments of counsel.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. (see (MPEP 716.01(c)).

Applicant is informed that this is not an invitation to submit a Declaration in response to this Office Action because a Declaration submitted after Final Office Action would not be considered timely (see (MPEP § 716.01).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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